

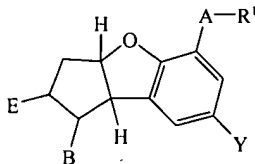
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claims 1-3 (Canceled).

Claim 4. (Currently amended) A sustained-release pharmaceutical composition comprising an ionic prostaglandin I₂ derivative of the following general formula (I):



and an ionic compound having an opposite charge to that of the ionic prostaglandin I₂ derivative **and increasing, which increases** the oil/water partition coefficient of the ionic prostaglandin I₂ derivative,

wherein

R¹ represents COOR² (wherein R² represents:

- 1) hydrogen or a pharmacologically acceptable cation,
 - 2) -Z-Ar¹, wherein Z is a valence bond or a straight or branched alkylene shown by C_tH_{2t} wherein t is an integer of 1 to 6, and Ar¹ is 2-pyridyl, 3-pyridyl or 4-pyridyl;
 - 3) -C_tH_{2t}COOR³, wherein C_tH_{2t} has the same significance as defined above, and R³ is hydrogen or a pharmacologically acceptable cation;
- or,
- 4) -C_tH_{2t}N(R⁴)₂, wherein C_tH_{2t} has the same significance as defined above, and R⁴ is hydrogen, a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms);

A represents:

- 1) -(CH₂)_m-, wherein m is an integer of 1 to 3;
- 2) -CH=CH-CH₂;

- 3) $-\text{CH}_2-\text{CH}=\text{CH}-$;
- 4) $-\text{CH}_2-\text{O}-\text{CH}_2-$;
- 5) $-\text{CH}=\text{CH}-$;
- 6) $-\text{O}-\text{CH}_2-$; or,
- 7) $-\text{C}\equiv\text{C}-$;

Y represents hydrogen, an alkyl having 1 to 4 carbon atoms, chlorine, bromine, fluorine, formyl, methoxy or nitro;

B represents $-\text{X}-\text{C}(\text{R}^5)(\text{R}^6)\text{OR}^7$ (wherein R^5 represents hydrogen or an alkyl having 1 to 4 carbon atoms; R^7 represents hydrogen, an acyl having 1 to 14 carbon atoms, an aroyl having 6 to 15 carbon atoms, tetrahydropyranyl, tetrahydrofuranyl, 1-ethoxyethyl or t-butyl; X represents:

- 1) $-\text{CH}_2-\text{CH}_2-$;
- 2) $-\text{CH}=\text{CH}-$; or
- 3) $-\text{C}\equiv\text{C}-$;

R^6 represents:

- 1) a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms;
- 2) $-\text{Z}-\text{Ar}^2$ wherein Z has the same significance as defined above and Ar^2 is phenyl, α -naphthyl, β -naphthyl or a phenyl substituted with at least one of chlorine, bromine, fluorine, iodine, trifluoromethyl, an alkyl having 1 to 4 carbon atoms, nitro, cyano, methoxy, phenyl or phenoxy;
- 3) $-\text{C}_t\text{H}_{2t}\text{OR}^8$, wherein C_tH_{2t} has the same significance as defined above, and R^8 is a straight alkyl having 1 to 6 carbon atoms, a branched alkyl having 3 to 6 carbon atoms, phenyl, a phenyl substituted with at least one of chlorine, bromine, fluorine, iodine, trifluoromethyl, an alkyl having 1 to 4 carbon atoms, nitro, cyano, methoxy, phenyl or phenoxy, cyclopentyl, cyclohexyl, or a cyclopentyl or cyclohexyl substituted with 1 to 4 straight alkyl group(s) having 1 to 4 carbon atoms;

- 4) $-Z-R^9$, wherein Z has the same significance as defined above, and R^9 is hydrogen, a cycloalkyl having 3 to 12 carbon atoms or a substituted cycloalkyl having 3 to 12 carbon atom which is substituted with 1 to 3 alkyl groups having 1 to 5 carbon atoms;
- 5) $-C_tH_{2t}-CH=C(R^{10})R^{11}$, wherein C_tH_{2t} has the same significance as defined above, and R^{10} and R^{11} represent hydrogen, methyl, ethyl, propyl or butyl;
or
- 6) $-C_uH_{2u}-C\equiv C-R^{12}$, wherein u is an integer of 1 to 7, C_uH_{2u} is a straight or branched alkylene and R^{12} is a straight alkyl having 1 to 6 carbon atoms);
- E represents hydrogen or OR^{13} , wherein R^{13} is hydrogen, an acyl having 1 to 12 carbon atoms, an aroyl having 7 to 18 carbon atoms, a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms; or a salt thereof.

Claim 5. (Canceled).

Claim 6. (Previously Presented) A sustained-release pharmaceutical composition according to claim 4, wherein the ionic compound is incorporated at least in an equimolar amount based on the ionic prostaglandin I_2 derivative in terms of a charge ratio.

Claim 7. (Previously Presented) A sustained-release pharmaceutical composition according to claim 4, wherein the ionic prostaglandin I_2 derivative is anionic.

Claim 8. (Original) A sustained-release pharmaceutical composition according to claim 7, wherein the ionic compound is a compound containing a group selected from an ammonium, pyridinium, phosphonium and sulfonium group in the molecule thereof, or a salt thereof.

Claim 9. (Original) A sustained-release pharmaceutical composition according to claim 8, wherein the ionic compound contains at least one member selected from the group consisting of an alkyldimethylbenzylammonium salt, an alkyltrimethylammonium salt, an alkylpyridinium salt, an alkylamine salt and an alkylphosphonium salt.

Claim 10. (Original) A sustained-release pharmaceutical composition according to claim 9, wherein the ionic compound is benzalkonium chloride.

Claim 11. (Canceled).

Claim 12. (Previously Presented) A sustained-release pharmaceutical composition according to claim 4, wherein the prostaglandin I₂ derivative is (±)-(1R*-2R*, 3aS*, 8bS*)-2,3,3a,8b-tetrahydro-2-hydroxy-1-[(E)-(3D*)-3-hydroxy-4-methyl-1-octen-6-ynyl]-1H-cyclopenta[b]benzofuran-5-butanoic acid, or a salt thereof.

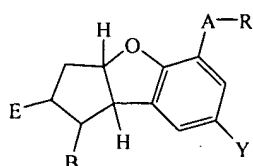
Claim 13. (Previously Presented) A sustained-release pharmaceutical composition according to claim 4, wherein the ionic prostaglandin I₂ derivative is cationic.

Claim 14. (Original) A sustained-release pharmaceutical composition according to claim 13, wherein the ionic compound is a compound containing a carboxyl, sulfate, sulfonate or phosphate group in the molecule thereof, or a salt thereof.

Claim 15. (Original) A sustained-release pharmaceutical composition according to claim 14, wherein the ionic compound is sodium lauryl sulfate and/or sodium oleate.

Claim 16. (Canceled).

Claim 17. (Previously Presented) A sustained-release pharmaceutical composition for a cationic ionic prostanoic acid derivative comprising an prostanoic acid derivative and an ionic compound having an opposite charge to that of the ionic prostanoic acid derivative and increasing hydrophobicity of the prostanoic acid derivative, wherein said ionic compound contains a carboxyl, sulfate, sulfonate or phosphate group in the molecule thereof, or a salt thereof, and wherein said prostaglandin I₂ derivative is of the formula:



wherein

R¹ represents COOR² (wherein R² represents:

- 1) hydrogen or a pharmacologically acceptable cation,
- 2) -Z-Ar¹, wherein Z is a valence bond or a straight or branched alkylene shown by C_tH_{2t}, wherein t is an integer of 1 to 6, and Ar¹ is 2-pyridyl, 3-pyridyl or 4-pyridyl;
- 3) -C_tH_{2t}COOR³, wherein C_tH_{2t} has the same significance as defined above, and R³ is hydrogen or a pharmacologically acceptable cation;

or,

- 4) -C_tH_{2t}N(R⁴)₂, wherein C_tH_{2t} has the same significance as defined above, and R⁴ is hydrogen, a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms);

A represents:

- 1) -(CH₂)_m-, wherein m is an integer of 1 to 3;
- 2) -CH=CH-CH₂;
- 3) -CH₂-CH=CH-;
- 4) -CH₂-O-CH₂-;
- 5) -CH=CH-;
- 6) -O-CH₂-; or,

7) $C \equiv C-$;

Y represents hydrogen, an alkyl having 1 to 4 carbon atoms, chlorine, bromine, fluorine, formyl, methoxy or nitro;

B represents $-X-C(R^5)(R^6)OR^7$ (wherein R^5 represents hydrogen or an alkyl having 1 to 4 carbon atoms; R^7 represents hydrogen, an acyl having 1 to 14 carbon atoms, an aroyl having 6 to 15 carbon atoms, tetrahydropyranyl, tetrahydrofuranyl, 1-ethoxyethyl or t-butyl; X represents:

- 1) $-CH_2-CH_2-$;
- 2) $-CH=CH-$; or
- 3) $-C \equiv C-$;

R^6 represents:

- 1) a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms;
- 2) $-Z-Ar^2$ wherein Z has the same significance as defined above and Ar^2 is phenyl, α -naphthyl, β -naphthyl or a phenyl substituted with at least one of chlorine, bromine, fluorine, iodine, trifluoromethyl, an alkyl having 1 to 4 carbon atoms, nitro, cyano, methoxy, phenyl or phenoxy;
- 3) $-C_tH_{2t}OR^8$, wherein C_tH_{2t} has the same significance as defined above, and R^8 is a straight alkyl having 1 to 6 carbon atoms, a branched alkyl having 3 to 6 carbon atoms, phenyl, a phenyl substituted with at least one of chlorine, bromine, fluorine, iodine, trifluoromethyl, an alkyl having 1 to 4 carbon atoms, nitro, cyano, methoxy, phenyl or phenoxy, cyclopentyl, cyclohexyl, or a cyclopentyl or cyclohexyl substituted with 1 to 4 straight alkyl group(s) having 1 to 4 carbon atoms;
- 4) $-Z-R^9$, wherein Z has the same significance as defined above, and R^9 is hydrogen, a cycloalkyl having 3 to 12 carbon atoms or a substituted cycloalkyl having 3 to 12 carbon atom which is substituted with 1 to 3 alkyl groups having 1 to 5 carbon atoms;

- 5) $-C_tH_{2t}-CH=C(R^{10})R^{11}$, wherein C_tH_{2t} has the same significance as defined above, and R^{10} and R^{11} represent hydrogen, methyl, ethyl, propyl or butyl;
or
- 6) $-C_uH_{2u}-C\equiv C-R^{12}$, wherein u is an integer of 1 to 7, C_uH_{2u} is a straight or branched alkylene and R^{12} is a straight alkyl having 1 to 6 carbon atoms);
E represents hydrogen or OR^{13} , wherein R^{13} is hydrogen, an acyl having 1 to 12 carbon atoms, an aroyl having 7 to 18 carbon atoms, a straight alkyl having 1 to 12 carbon atoms or a branched alkyl having 3 to 14 carbon atoms; or a salt thereof.

Claim 18. (Previously Presented) A sustained-release pharmaceutical composition according to claim 17, wherein the ionic compound is sodium lauryl sulfate and/or sodium oleate.